

# Using Real-World Evidence to Support Regulatory Submissions

Best practices and Learnings

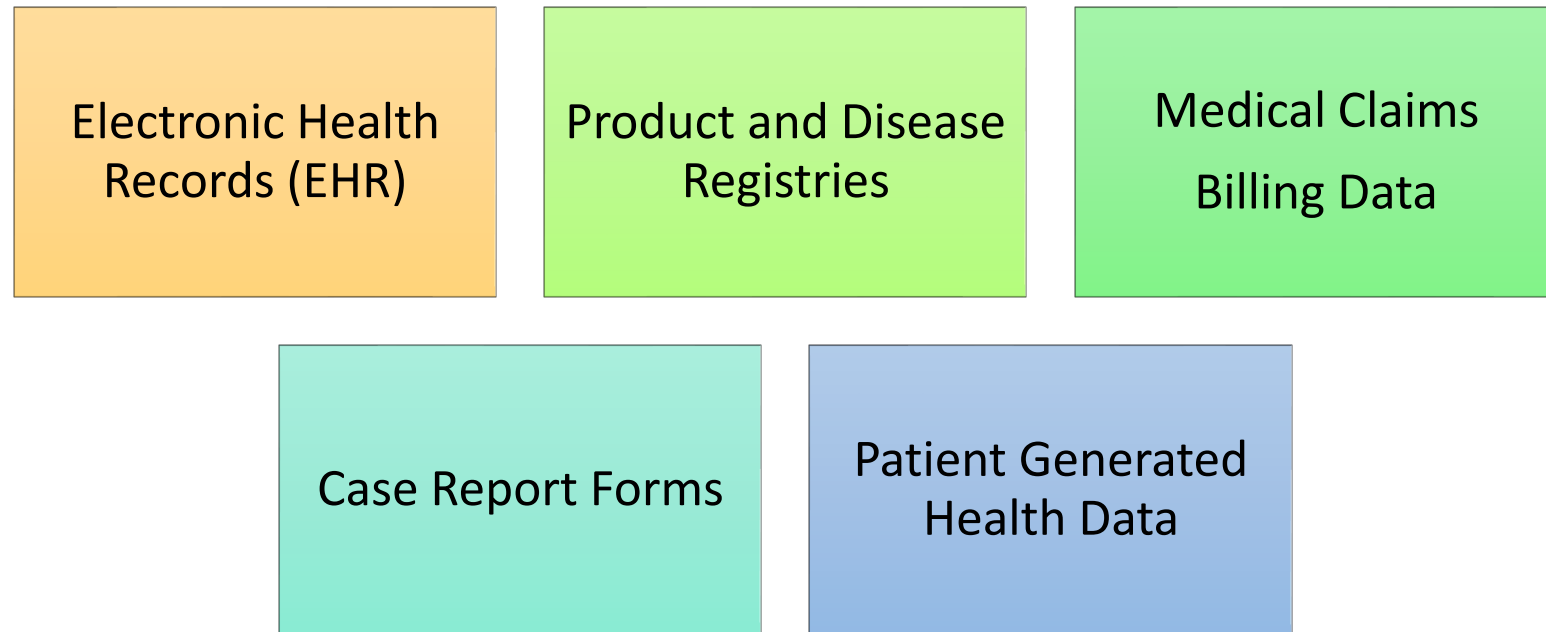
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# Real World Data (RWD)

## Definition and Sources

- Data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources



# Real World Evidence (RWE)

Generating evidence from RWD

- Clinical evidence about the usage and potential benefits or risks of a medical device derived from analysis of RWD

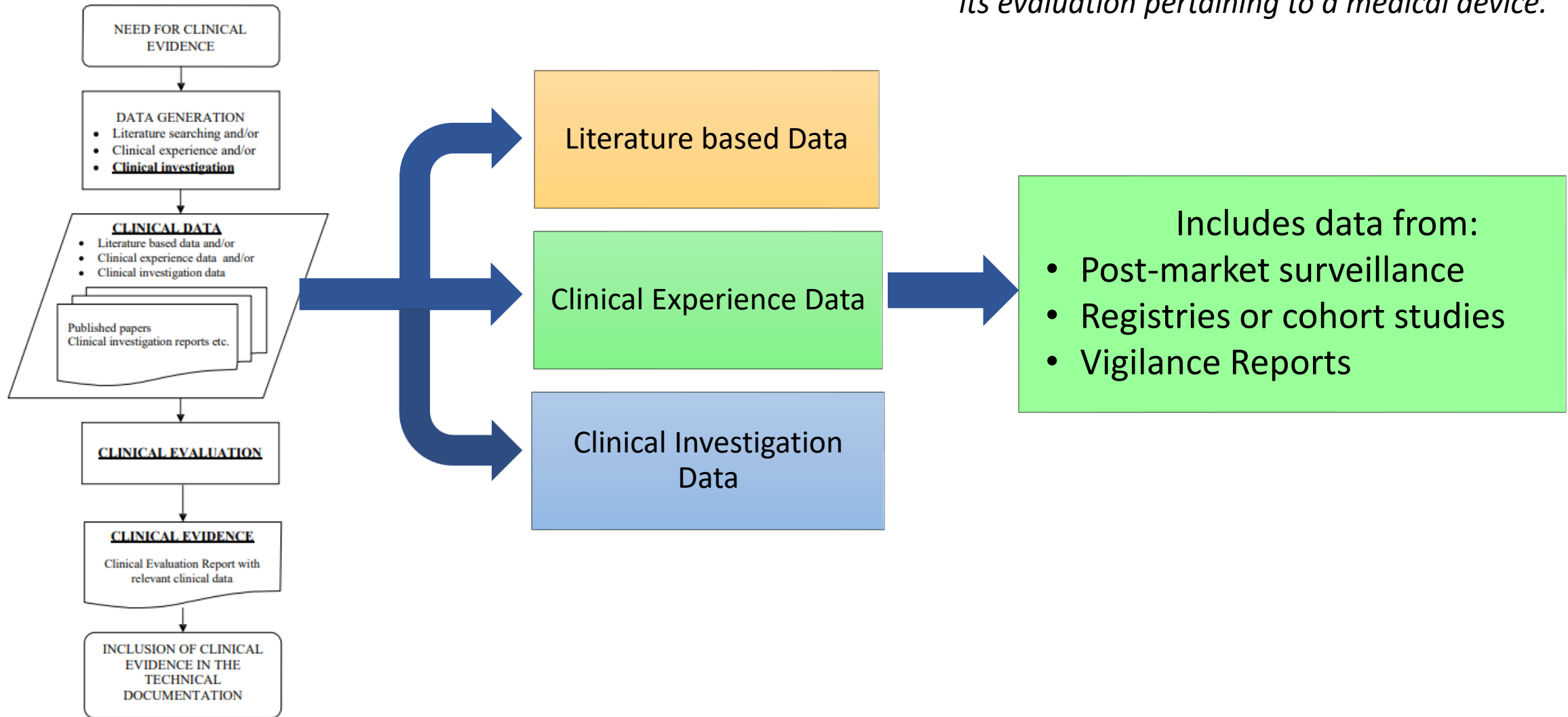


- **Quality of the RWD source** – *fit for purpose, completeness, accuracy, representative*
- **Design of the studies used to generate RWE** – *appropriate statistical methods, potential bias, hypothesis generation, sample size, well controlled studies*
- **Replicability and transparency** – *Possible to duplicate study with similar data*

# Clinical Evidence for medical devices

## Clinical Experience Data in Clinical Evaluation Report

*\*Clinical evidence refers to the clinical data and its evaluation pertaining to a medical device.*



# Clinical Trials vs Real World Data

Understanding the key differences

## Clinical Trials

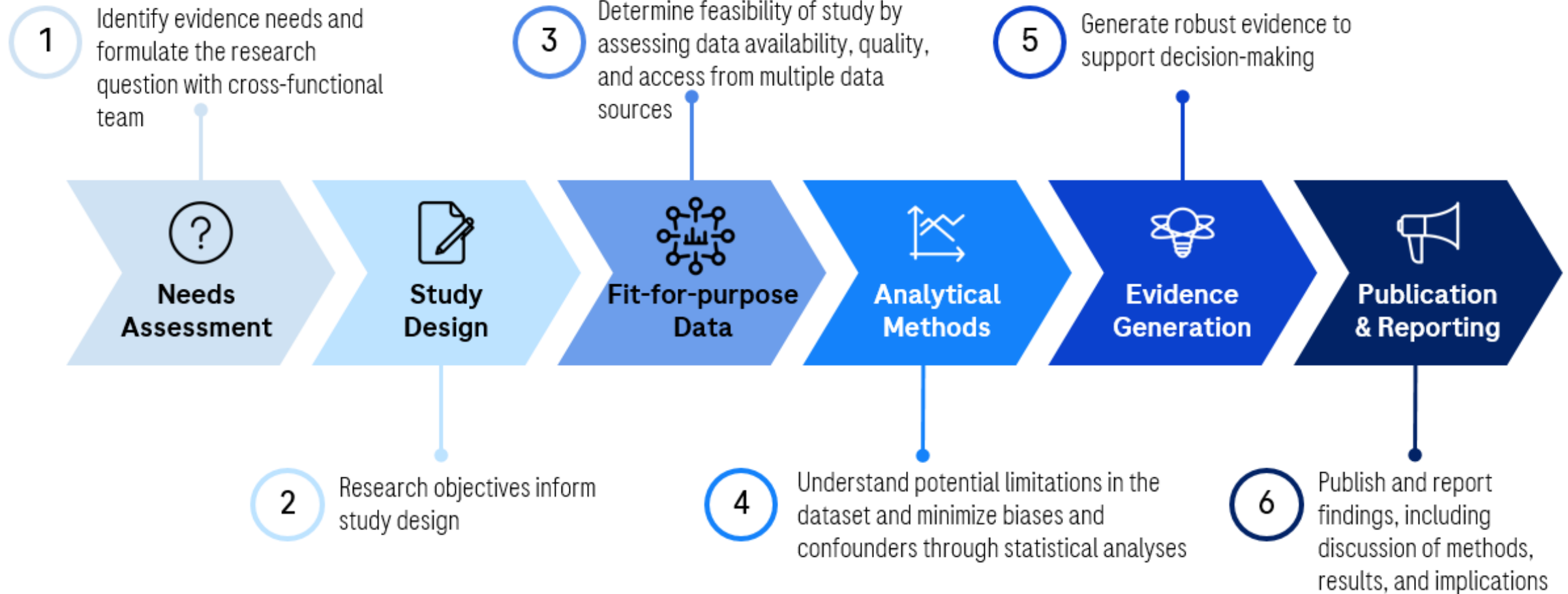
- Homogenous population; smaller or limited sample size
- Special sites under controlled conditions
- Interventions and treatments per protocol
- Prespecified outcomes over defined time period
- Data collected at predefined time points per protocol
- Randomized to minimize bias


## RWD

- Diverse real world population; data from wider population
- Routine care settings
- Reflects variabilities in treatment patterns
- Broader outcomes over longer duration
- Data from routine care such as those captured in patient records
- Observational in nature

# Conducting a RWD study involves scientific rigor at each step

Maintaining robust methodology and promoting transparency and traceability are key



 **Not all research questions can be addressed using RWD. All studies follow and respect the required compliance processes.**

# RWD studies can bridge the evidence gaps from traditional studies

However, it is important to keep in mind certain limitations when interpreting the results and



## Real-world data is valuable complement to other forms of evidence

- Reflects **routine clinical practice**
- May describe a **large and diverse** patient population
- May encompass a **wide range of data types** (structured, free text, image, genomic, etc.) and allows for **longitudinal observation**
- Complements other forms of evidence to potentially **provide patient access** to innovative diagnostic solutions



## Inherent challenges of real-world data

- Real-world data is usually **not collected with the intent to answer a specific research question or hypotheses**
- **Data source variability** poses challenges in establishing a standardized way to assess data quality
- **Segmented data and restrictions on data access** add further complexities when working with fit-for-purpose data in the regulatory context

# Regulators around the world are embracing Real-World Data

However, many challenges persist in the actual utilization of Real-World Data (RWD) for regulatory purposes

## Opportunities



**Numerous published guidances**



**Increased RWD awareness and willingness to consider RWE**



**Launch of many RWD pilot & demonstration projects**

## Challenges



- Guidances are broad and lack specificity
- Fewer Real-World Evidence (RWE) guidances specific to *In Vitro* Diagnostics (IVDs) and relatively new for digital health
- Despite overlaps, definitions and requirements vary across regulators
- Variability and complexities in the execution of use cases



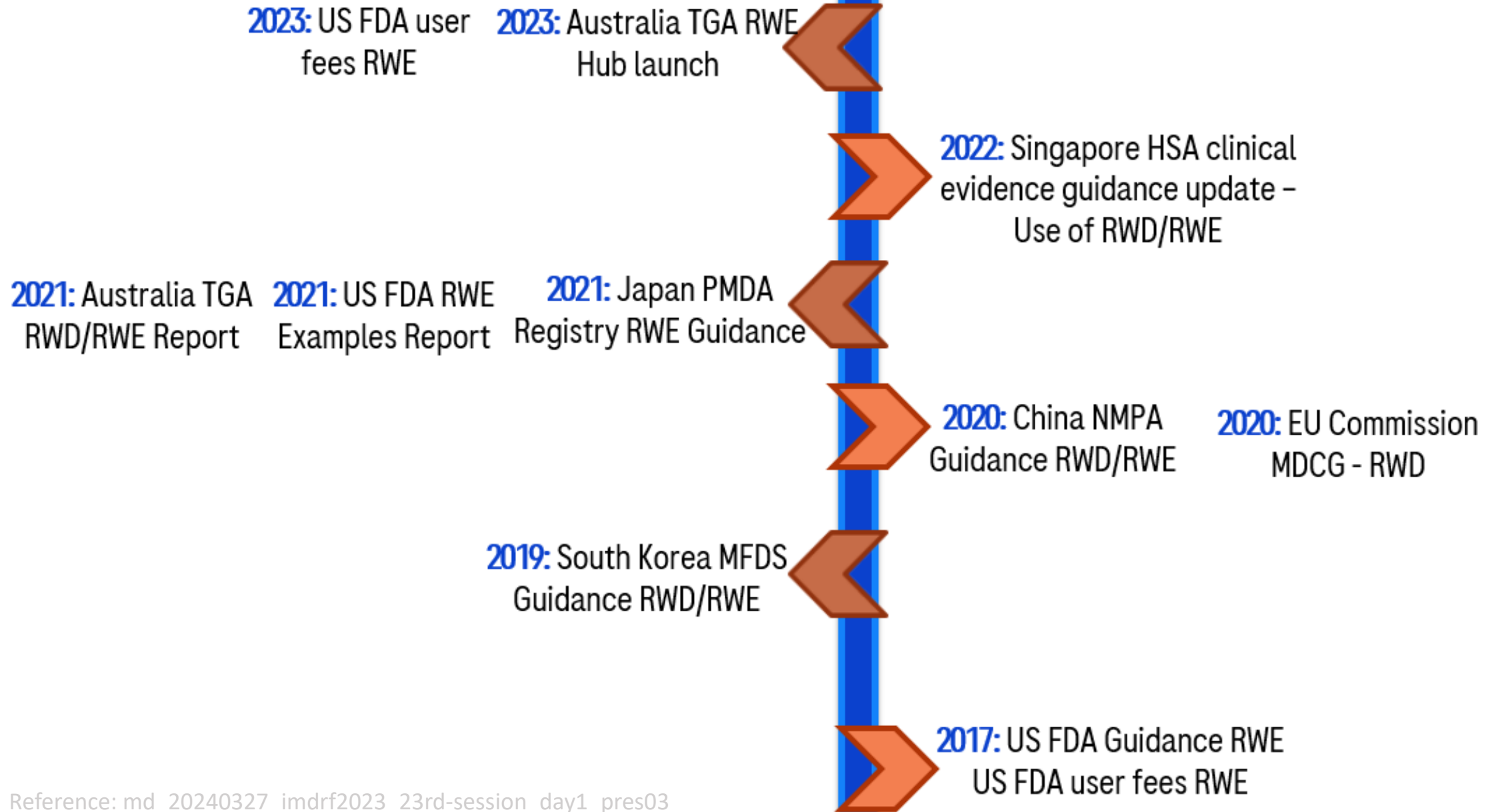
- Questions around methods and quality remain
- Obstacles around risk acceptance and determining “acceptable” level of uncertainty



- Execution is challenging due to lack of guidance specificity and risk associated with pilots for sponsors
- Need for real-time and regular interactions with relevant expertise (on the sides of both sponsors and agencies) to ensure relevant and timely input for RWD studies

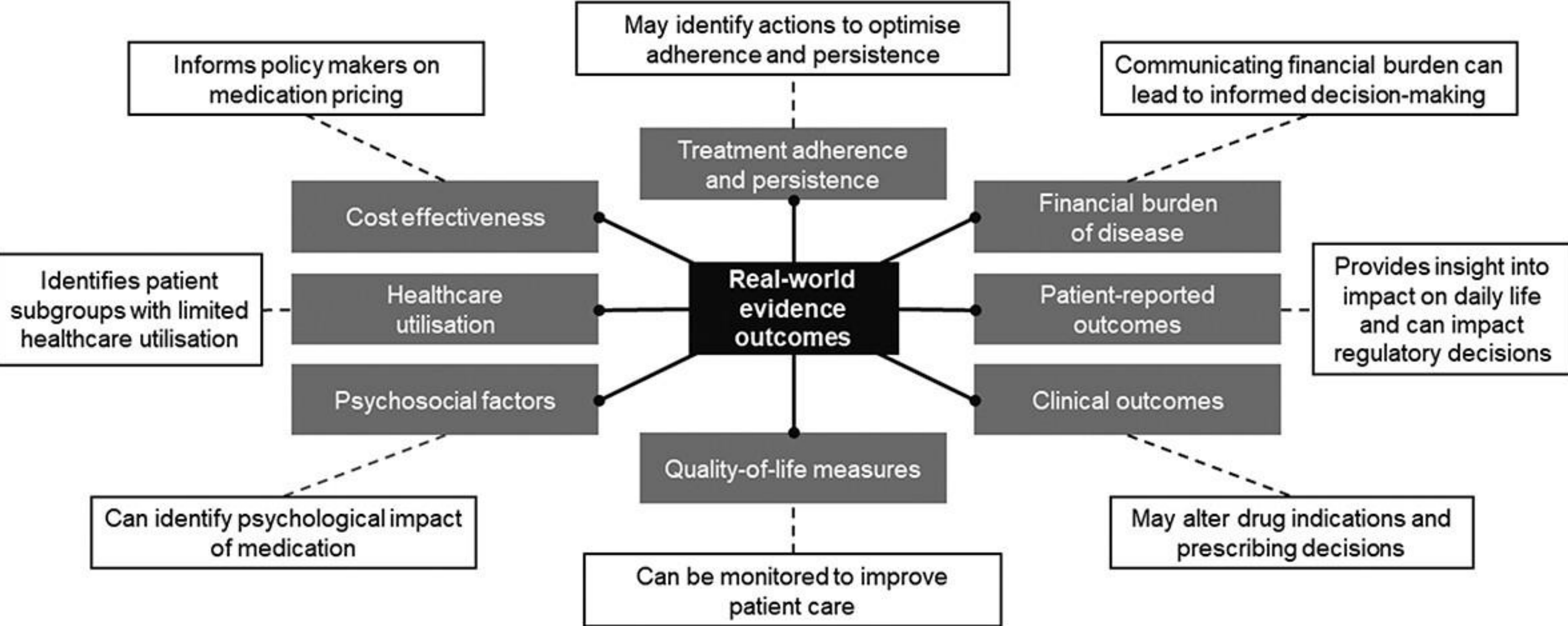


# Timeline for Key RWE activities



# Practical applications of RWE in healthcare

Numerous possibilities



Source: EXPERT OPINION ON DRUG SAFETY 2023, VOL. 22, NO. 6, 443–445

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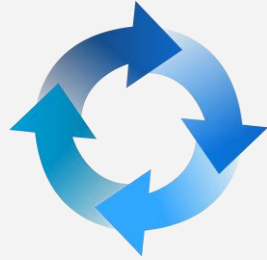
# RWD regulatory use cases

Leveraging RWD to support regulatory submissions



## EVIDENCE

Supplement clinical trial data for regulatory, HTA and payment decisions



MD lifecycle data to support new indications, improvements



Postmarket Surveillance, safety, effectiveness and utilisation data



Novel MDs and IVDs – Strengthening Clinical Evidence



Risk stratification and management programs for healthcare systems



Support good use practices for MDs, Clinical guidelines from professional societies

# RWD can generate powerful insights to support regulatory decisions

However, due to RWD-specific considerations, an exact match with clinical studies cannot be expected

Yielding impactful insights to inform regulatory decision-making



## Complementary evidence:

RWE generated can serve as valuable complementary evidence to those generated from clinical studies



**Additional insight:** RWD can sometimes provide insights not available from traditional clinical studies (e.g., special population)



**RWD collection:** Due to their non-interventional nature, inability to precisely control what RWD the sites/labs collect and how they collect



**Additional considerations for IVDs:** Due to the level of complexity introduced by reagents, calibrators, analyzers, control materials, and specimen types



**Evolving populations & guidelines:** Changing populations (e.g., due to successful vaccination campaigns) and expanded knowledge/updated guidelines can impact the design of the study (e.g., neonatal sepsis - age specific cutpoints, quickly evolving COVID-19 standard of care and reference comparator )



Additional considerations for IVD studies

# Key takeaways from regulatory submissions with RWD

How can we further advance the use of RWD in supporting regulatory decisions?

## Main Learnings



- **Despite uncertainties** inherently present in RWD, **conclusions can still be drawn** as long as the proper methodologies have been applied to generate robust evidence



- **Transparency and documentation** in the data management lifecycle (e.g., evaluation, extraction, flow, etc.) and study processes (e.g., study design, analysis, reporting) are key to promoting successful submissions



- Overall, **pre-submission discussions have served as valuable opportunities** in gathering early and specific feedback from the regulatory authority

# Thank you